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EXAMINER	
JUNG, UNSU	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,740	CAUWENBERGHS ET AL.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-41 and 46-59* is/are pending in the application.

4a) Of the above claim(s) *46 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-41 and 48-59* is/are rejected.

7)☒ Claim(s) *32,39,48 and 49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 May 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment to the specification in the reply filed on September 9, 2005 is acknowledged and entered.

2. Applicants' amendments to the claims in the reply filed on September 9, 2005 is acknowledged.

Election/Restrictions

3. Applicants' election with traverse of Group I and Group VI in the reply filed on September 9, 2005 is acknowledged. The traversal is on the ground(s) that an international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn to a process and an apparatus or means specifically designed for carrying out the process. Applicants further submit that Group I and Group VI claims, as amended, share a novel special technical feature in compliance with 37 C.F.R. §1.475(a), i.e., the use of a soluble form or a portion of glycoprotein 1b(α) and a ristocetin or a functionally equivalent substance for detecting von-Willebrand disease and that this special teancial feature is novel over Murata et al. (J. Biol. Chem., 1991, Vol. 266, pp015474-15480). Applicants suggest that Murata et al. does not teach or suggest the use of a soluble form or a portion of glycoprotein 1b(α). This is not found persuasive because the special technical feature of Groups I and VI is a soluble form or a portion of glycoprotein

1b(α) and a ristocetin or a functionally equivalent substance. As stated in the Office Action filed on June 14, 2005, these elements cannot be a special technical feature under PTC Rule 13.2 because the elements are shown in the prior art. Murata et al. (J Biol Chem, 1991, Vol. 266, pp15474-15480) teaches the use of a soluble form (p15475, column 2, *^{125}I-vWF Binding to Immobilized Recombinant GP Ibα*, lines 8-9) or portion of GPIb(α), ristocetin, and an antibody in an assay to determine vWF binding to immobilized recombinant glycoprotein 1b(α) (Abstract and p15475, column 2, *^{125}I-vWF Binding to Immobilized Recombinant GP Ibα*, lines 5-28).

The requirement is still deemed proper and is therefore made FINAL.

Drawings

4. The drawings are objected to because of the following reasons:

Fig. 1: the reference symbols, Δ for 500 μg/ml and ∇ for 250 μg/ml ristocetin, in the figure legend on p14, lines 18-19 of the specification are different from the symbols in Fig. 1 as the triangles are in a closed form.

Fig. 3: the reference symbol •, indicating a binding curve of plasma VWF to the rGPIbα-fragment in the presence of 760 μg/ml, in the figure legend on p15, lines 22-24 of the specification is different from the symbol, ■, in Fig. 3.

Fig. 4: the shaded bars representing vWF:Ag are not distinguishable from the black bars representing vWF:RiCof

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

5. The use of the trademarks ULTROSER® (p18, line 12) and SEPHAROSE® (p18, line 27) have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

6. Claim 32 is objected to because of the following informalities: the phrase "von-Willebrand factor" in lines 1-2 has already been abbreviated in claim 1, lines 3-4. Therefore, abbreviated form of the phrase "von-Willebrand factor", vWF, should be used subsequently. Appropriate correction is required.

7. Claim 39 is objected to because of the following informalities: the phrase "the group" in lines 2-3 should be corrected to "a group". Appropriate correction is required.

8. Claims 48 and 49 are objected to because of the following informalities: the phrase "von-Willebrand disease" in lines 1-2 has already been abbreviated in claim 1, lines 1-2. Therefore, abbreviated form of the phrase "von-Willebrand disease", vWD, should be used subsequently. Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 53 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 53 recites that the solid support is selected from a group consisting of plastic, glass, silicon, metal, polystyrene, polyvinyl chloride, polypropylene, polyethylene, polycarbonate, dextran, nylon, amylose, natural or modified cellulose, polyacrylnmide, agarose, magnetide and any combinations thereof. Applicants refer to p10, lines 21-31 for the support for the new claim 53. However, plastic and silicon are not found on the list of materials comprising the solid support in the current specification.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 31-41 and 48-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. In claim 31, the phrases "vWF-activity" and "vWF-antigen" in step c) are vague and indefinite. It is not clear whether or not the phrases "vWF-activity" and "vWF-antigen" in step c) refers to the "vWF-activity" in step a) and "vWF-antigen" in step b), respectively.

14. Claim 32 recites the limitation "the formation" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 31-33, 35, 37-41, 48, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463).

Favaloro et al. teaches a method for detecting von-Willebrand disease (vWD) comprising the steps of (Abstract):

a) detecting von-Willebrand factor (vWF) activity in a sample (p153, right column, *Collagen binding assay for vWF*);

b) determining the amount of vWF-antigen in the sample (p153, left column, *ELISA assay for vWF:Ag*);

c) determining the ratio between vWF-activity and vWF-antigen for the sample (Abstract);

d) comparing the ratio obtained under c) to a range of ratios established as normal range (p154, Table 1);

e) detecting vWD based on the comparison result obtained under step (d) (Abstract).

However, Favaloro et al. fails to teach a detection step of a) comprising a soluble form or a portion of glycoprotein 1b(α) (GP1b(α)) and ristocetin or a functionally equivalent substance.

Hoylaerts et al. teaches a method of detecting vWF activity in a sample (human plasma) using a soluble form or a portion of glycoprotein 1b(α) (GP1b(α)) and ristocetin (p454, *Purification of GPIb*, *Purification of wWF*, and *Studies of Interaction between vWF and GPIb*). Hoylaerts et al. teaches that the ristocetin-mediated vWF binding to immobilized GPIb is a reversible event (p457, right column, *Specificity of ristocetin-mediated vWF binding to GPIb*, lines 1-3). Therefore, coated GPIb is considered suitable for the study of ristocetin-dependent interactions between GPIb and vWF (p457, right column, *Specificity of ristocetin-mediated vWF binding to GPIb*, lines 4-6). To study this binding quantitatively, pure-GPIb-coated microtiter plates potentially offered an advantage over agglutination studies with formalin fixed platelets, in which ristocetin-mediated interactions with other platelet proteins participate (p457, right column, *Specificity of ristocetin-mediated vWF binding to GPIb*, lines 6-10).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Favaloro et al. with the method of detecting vWF activity in a sample using a soluble form or a portion of glycoprotein 1b(α) (GP1b(α)) and ristocetin as taught by Hoylaerts et al. in order to quantitatively study ristocetin-mediated vWF binding to immobilized GPIb, which has an advantage over agglutination studies with formalin fixed platelets, in which ristocetin-mediated interactions with other platelet proteins participate.

With respect to claim 32, Hoylaerts et al. teaches a method of detecting vWF activity comprising detecting a formation of a complex of vWF and GP1b(α) (p p454,

Purification of GPIb, *Purification of wWF*, and *Studies of Interaction between vWF and GPIb*).

With respect to claim 33, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the method of detecting vWF activity, wherein is bound to a solid support (p454, left column, *Studies of Interaction between vWF and GPIb*, lines 2-5).

With respect to claim 35, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the complex of vWF and GP1b(α) is bound to a solid support (p454, *Purification of GPIb*, *Purification of wWF*, and *Studies of Interaction between vWF and GPIb*).

With respect to claim 37, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the detecting vWF activity under step a) comprises using an anti-vWF antibody (p454, right column, lines 30-33).

With respect to claims 38 and 39, Hoylaerts et al. teaches a method of detecting vWF activity under step a) comprising an ELISA (p454, right column, lines 30-33).

With respect to claim 40, Favaloro et al. teaches a method of detecting vWF activity under step a) using a homogeneous agglutination assay (p153, right column, *Ristocetin cofactor assay*).

With respect to claim 41, Favaloro et al. teaches a method, wherein the sample is obtained from plasma of a patient (p152, right column, *Introduction*, lines 4-9).

With respect to claims 48 and 49, Favaloro et al. teaches a method, wherein detecting vWD under step e) comprises discriminating between type 1 and type 2 vWD (p153, left column, *Introduction*, lines 17-23).

19. Claims 34, 36, 50-53, and 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463) as applied to claims 31-33 and 35 above, and further in view of Handin (U.S. Patent No. 5,321,127, Filed Mar. 18, 1991).

Favaloro et al. in view of Hoylaerts et al. teaches a method for detecting vWD. However, Favaloro et al. in view of Hoylaerts et al. fails to teach a method, wherein the GP1b(α) is bound to the solid support by an anti- GP1b(α) antibody.

Handin teaches a method of obtaining human platelet GP1b(α) receptor fragments containing the vWF binding site (column 3, lines 5-11) and antibody against the GP1b(α) receptor fragment. Handin teaches that the antibodies and substantially purified antigen can be incorporated in a kit form such as ELISA (column 11, line 61-column 12, line 7), which involves immobilized antibodies either covalently or physically bound to a solid phase immunoadsorbent such as glass, polystyrene, polypropylene, dextran, nylon, and other materials in the form of tubes, beads, and microtiter plates (column 12, lines 47-61). Those skill in the art will appreciate that antibodies will be useful in other variations and forms of assays, which are presently known or may be developed in the future (column 12, lines 12-17).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Favaloro et al. in view of Hoylaerts et al. with the method of immobilizing antibodies against a GP1b(α) receptor fragment on a

solid immunoadsorbent surface as taught by Handin in order to specifically immobilize GP1b(α) receptor fragment containing the vWF binding site to perform other variations and forms of assays, which are presently known, such as a detection assay for determining vWF activity in a sample.

With respect to claim 36, Handin teaches a method of immobilizing anti- GP1b(α) antibody to a solid support (column 12, lines 47-61), which can be used in the detection assay for determining vWF activity, wherein a complex of vWF and GP1b(α) is formed as taught by Hoylaerts et al. (p454, *Studies of interaction between vWF and GPIb*).

With respect to claim 50, Handin teaches a method of obtaining a recombinant human platelet GP1b(α) receptor fragments containing the vWF binding site (column 3, lines 5-11).

With respect to claim 51, Handin teaches that the antibody against the GP1b(α) receptor fragment is a monoclonal antibody (column 9, lines 43-44).

With respect to claim 52, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the detecting vWF activity under step a) comprises using an anti-vWF antibody, which is detectably labeled (p454, right column, lines 30-33).

With respect to claim 53, Handin teaches a solid support, which is selected from a group consisting of glass, polystyrene, polypropylene, dextran, and nylon (column 12, lines 47-61).

With respect to claim 56, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the sample is diluted (p454, left column, *Studies of interaction between vWF and GPIb*, lines 5-7).

With respect to claims 57-59, Handin teaches a method of immobilizing anti-GP1b(α) antibody to a solid support (column 12, lines 47-61), which can be used in the detection assay for determining vWF activity, wherein a complex of vWF and GP1b(α) is formed as taught by Hoylaerts et al. (p454, *Studies of interaction between vWF and GPIb*).

20. Claims 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463) and Handin (U.S. Patent No. 5,321,127, Filed Mar. 18, 1991) as applied to claim 53 above, and further in view of Elings et al. (U.S. Patent No. 4,537,861, Filed Feb. 3, 1983).

Favaloro et al. in view of Hoylaerts et al. and Handin teaches a method for detecting vWD. Handin teaches that the antibodies and substantially purified antigen can be incorporated in a kit form such as ELISA (column 11, line 61-column 12, line 7), which involves immobilized antibodies either covalently or physically bound to a solid phase immunoadsorbent such as glass, polystyrene, polypropylene, dextran, nylon, and other materials in the form of tubes, beads, and microtiter plates (column 12, lines 47-61). However, Favaloro et al. in view of Hoylaerts et al. and Handin fails to teach a method, wherein the solid support comprises a latex bead.

Elings et al. teaches a method of particle agglutination (aggregation) assay using a well known carrier such as latex particles coated with a specific antibody (column 10, lines 27-32).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Favaloro et al. in view of Hoylaerts et al. and Handin with the method of using latex particles (beads) coated with a specific antibody as taught by Elings et al. in order to perform a particle agglutination assay.

21. Claims 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463) as applied to claim 40 above, and further in view of Elings et al. (U.S. Patent No. 4,537,861, Filed Feb. 3, 1983).

Elings et al. teaches a method of particle agglutination (aggregation) assay using a well known carrier such as latex particles coated with a specific antibody (column 10, lines 27-32).

Favaloro et al. in view of Hoylaerts et al. teaches a method for detecting vWD. Favaloro et al. further teaches a method of detecting vWF activity under step a) using a homogeneous agglutination assay (p153, right column, *Ristocetin cofactor assay*). However, Favaloro et al. in view of Hoylaerts et al. fails to teach a method, wherein the agglutination is measured by electric field variation, magnetic field variation, turbidimetric variation or light scattering.

Elings et al. teaches a method of detecting agglutination (particle aggregation) using light scattering technique (column 10, lines 57-63).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Favaloro et al. in view of Hoylaerts et al.

with a method of using light scattering technique as taught by Elings et al. in order to detect agglutination (particle aggregation).

Conclusion

22. No claim is allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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